

### **Remarks**

Applicants thank the Examiner for the helpful interview held on September 23, 2003. Applicants agreed to amend claim 12 to delete references to cis (Z) isomers, and to resubmit paper #22, the Declaration under 37 C.F.R. § 1.132 of Dr. William Caldwell. Claim 12 has been amended (by submitting a structure that only reflects the trans (E) isomers) as agreed and paper #22 has been resubmitted.

### **Rejections under 35 U.S.C. § 103 (a)**

Claim 12 has been rejected under 35 U.S.C. § 103 (a) as obvious over U.S. Patent No. 5,597,919 to Dull et al. (Dull). The rejection is respectfully traversed.

The Office Action suggests that the previously submitted Declaration under 37 C.F.R. § 1.132 by Dr. William Caldwell only shows the unexpected/superior properties for pyridine compounds, not the claimed pyrimidinyl compound. As discussed with the Examiner, and as shown in the previously submitted Declaration under 37 C.F.R. § 1.132 by Dr. William Caldwell, compounds with a CH(CH<sub>3</sub>) group alpha to the terminal amine show acceptable binding to the relevant receptors, when compared to compounds with a CH<sub>2</sub> group alpha to the terminal amine. However, Applicants surprisingly determined that the compounds with the CH(CH<sub>3</sub>) group had improved resistance to monoamine oxidase, and therefore, had improved half-lives.

The effect of the alpha methyl group is on the alpha position relative to the terminal amine group. There is no sound scientific reason (or at least none has yet been presented) to believe that the alpha methyl effect would be present in pyridine compounds, but not in pyrimidine compounds. This is particularly true where the pyrimidine ring is relatively remote from the alpha methyl group (i.e., separated by three carbons). When this argument was discussed with the Examiner in the September 23, 2003 interview, agreement appeared to be reached regarding this issue.

The Office Action further stated that Dr. Caldwell's Declaration showed that R alpha-methyl isomers are as active as the unsubstituted compounds. While the Office Action did not go on to state that the S isomer was not believed to have the same activity, the Examiner alluded to this during the September 23, 2003 interview. With respect to the issue of R and S stereoisomers, as discussed with the Examiner, the Declaration supports the benefits of both

stereoisomers. For example, Table 5 of the Declaration shows the beneficial effects of both an R and an S isomer. Monoamine oxidase inhibition is observed regardless of the stereochemistry at the relevant carbon (alpha to the terminal amine). As this is believed to be a steric effect, there is no sound scientific reason (or, again, at least none has yet been submitted) to doubt that this is the case.

Further, the Office Action states that there is an issue regarding cis/trans isomers, in that the Declaration only taught the unexpected/superior properties of the trans isomers. Applicants have amended Claim 12 to refer to trans isomers (by amending the chemical structure in Claim 12), rather than cis and trans isomers, although they respectfully disagree with the Examiner's interpretation of the extent of the teachings in Dr. Caldwell's Declaration. Applicants reserve the right to pursue claims to the cis (Z) isomers in related cases, and state that since the cis (Z) compounds are useful compounds, the amendment was made solely to facilitate prosecution.

Accordingly, with respect to claim 12 as amended, Applicants respectfully request that the Examiner withdraw the rejections.

### **Rejections under Judicially Created**

#### **Doctrine of Obviousness-Type Double Patenting**

Claim 12 has been rejected under the judicially created doctrine of obviousness-type double patenting as being obvious over claim 8 of U.S. Patent No. 5,597,919. This rejection is respectfully traversed if applied to the amended claim, for the reasons stated above with respect to the obviousness rejection. As the Examiner is aware, the same obviousness standard applies under 35 U.S.C. § 103 or under the judicially created doctrine of obviousness-type double patenting. As the amendments and arguments presented above in connection with the same reference (U.S. Patent No. 5,597,919) obviate the rejection under 35 U.S.C. § 103, they also obviate the rejection under the judicially-created doctrine of obviousness-type double patenting.

Claim 12 has been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as obvious over claims 1-19 of co-pending U.S.S.N. 08/631,761. The '761 application has been abandoned, thus mooted the rejection. A copy of the notice of abandonment from the '761 application is attached.

Claim 12 has been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as obvious over claims 15-21 of co-pending U.S.S.N. 09/973,419. This rejection is respectfully traversed.

U.S.S.N. 09/973,419 has issued as U.S. Patent No. 6,555,684 to Caldwell et al. The application includes 7 claims (numbered as claims 15-21 when the application was pending). The Office Action indicated that the previously submitted terminal disclaimer had not been entered, but upon entry, would obviate the rejection. Applicants respectfully request that the terminal disclaimer be entered and the rejection be withdrawn.

### **Conclusion**

It is believed that Claim 12 as amended is in condition for allowance. Prompt receipt of a notice of allowance is respectfully requested. The Examiner is invited to contact the undersigned if he has any questions or further comments.

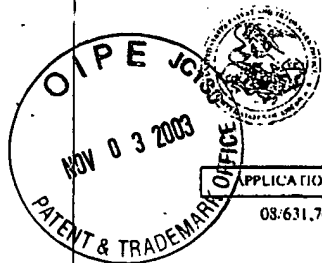
Respectfully submitted,



David S. Bradin  
Reg. No. 37,783  
Attorney for Applicant

Date: October 29, 2003

Womble Carlyle Sandridge & Rice, PLLC  
Post Office Box 7037  
Atlanta, Georgia 30357  
Telephone: (919) 484-2382  
Facsimile: (919) 484-2084



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1159  
Alexandria, Virginia 22313-1159  
www.uspto.gov

RECEIVED  
NOV 04 2003  
TECH CENTER 1600/2908

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/631,761	04/23/1996	WILLIAM S. CALDWELL	DD-129G	5535

7590 09/24/2003

CARL B. MASSEY, JR.  
WOMBI.FCARLYLE SANDRIDGE & RICE, P.L.L.C  
POST OFFICE BOX 7037  
ATLANA, GA 30357-0037

EXAMINER

RAO, DEEPAK R

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 09/24/2003

35

Please find below and/or attached an Office communication concerning this application or proceeding.




# Notice of Abandonment

Application No. <b>08/631,761</b>	Applicant(s) <b>Caldwell et al.</b>
Examiner <b>Deepak Rao</b>	Art Unit <b>1624</b>

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

This application is abandoned in view of:

1. ☒ Applicant's failure to timely file a proper reply to the Office letter mailed on Dec 27, 2002.
  - (a) ☐ A reply was received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the period for reply (including a total extension of time of \_\_\_\_\_ month(s)) which expired on \_\_\_\_\_.
  - (b) ☐ A proposed reply was received on \_\_\_\_\_, but it does not constitute a proper reply under 37 CFR 1.113(a) to the final rejection.  
(A proper reply under 37 CFR 1.113 to a final rejection consists only of: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114).
  - (c) ☐ A reply was received on \_\_\_\_\_ but it does not constitute a proper reply, or a bona fide attempt at a proper reply, to the non-final rejection. See 37 CFR 1.85(a) and 1.111. (See explanation in box 7 below).
  - (d) ☒ No reply has been received.
2. ☐ Applicant's failure to timely pay the required issue fee and publication fee, if applicable, within the statutory period of three months from the mailing date of the Notice of Allowance (PTOL-85).
  - (a) ☐ The issue fee and publication fee, if applicable, was received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the statutory period for payment of the issue fee (and publication fee) set in the Notice of Allowance (PTOL-85).
  - (b) ☐ The submitted issue fee of \$ \_\_\_\_\_ is insufficient. A balance of \$ \_\_\_\_\_ is due.  
The issue fee required by 37 CFR 1.18 is \$ \_\_\_\_\_. The publication fee, if required by 37 CFR 1.18(d) is \$ \_\_\_\_\_.
  - (c) ☐ The issue fee and publication fee, if applicable, has not been received.
3. ☐ Applicant's failure to timely file corrected drawings as required by, and within the three-month period set in, the Notice of Allowability (PTO-37).
  - (a) ☐ Proposed new formal drawings were received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the period for reply.
  - (b) ☐ No corrected drawings have been received.
4. ☐ The letter of express abandonment which is signed by the attorney or agent of record, the assignee of the entire interest, or all of the applicants.
5. ☐ The letter of express abandonment which is signed by an attorney or agent (acting in a representative capacity under 37 CFR 1.34(a)) upon the filing of a continuing application.
6. ☐ The decision by the Board of Patent Appeals and Interferences rendered on \_\_\_\_\_ and because the period for seeking court review of the decision has expired and there are no allowed claims.
7. ☐ The reason(s) below:

  
DEEPAK RAO  
PRIMARY EXAMINER  
ART UNIT 1624

Petitions to revive under 37 CFR 1.137(a) or (b), or requests to withdraw the holding of abandonment under 37 CFR 1.181, should be promptly filed to minimize any negative effects on patent term.